Guidance For Industry

Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Antibody to Hepatitis C Virus (Anti-HCV); (2) Supplemental Testing, and the Notification of Consignees and Blood Recipients of Donor Test Results for Anti-HCV

Comments and suggestions regarding this document may be submitted anytime to Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, room 1-23, Rockville, MD 20857. All comments should be identified by docket number 98D-0143. For questions regarding this document, contact Robin Biswas, M.D. by telephone at (301) 827-3011, or by telefax at (301) 496-0338.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
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GUIDANCE FOR INDUSTRY[1]: CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS: (1) QUARANTINE AND DISPOSITION OF UNITS FROM PRIOR COLLECTIONS FROM DONORS WITH REPEATEDLY REACTIVE SCREENING TESTS FOR ANTIBODY TO HEPATITIS C VIRUS (ANTI-HCV); (2) SUPPLEMENTAL TESTING, AND THE NOTIFICATION OF CONSIGNEES AND BLOOD RECIPIENTS OF DONOR TEST RESULTS FOR ANTI-HCV

I. INTRODUCTION

This document contains guidance that supersedes the HCV sections of the Food and Drug Administration (FDA) memorandum of July 19, 1996, entitled, "Recommendations for the Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Human T-Lymphotropic Virus Type I (HTLV-I)." Additionally, this guidance replaces FDA's guidance issued on March 20, 1998 entitled, "Guidance for Industry: Supplemental Testing and the Notification of Consignees of Donor Test Results for Antibody to Hepatitis C Virus (Anti-HCV)," which was withdrawn on September 8, 1998.

The FDA recommendations contained in this document are provided to enable quarantine and disposition of units from prior collections from donors with repeatedly reactive screening tests for HCV. Additionally**,** FDA recommends that consignees of certain blood and blood component units collected since January 1, 1988, which were anti-HCV negative or untested, be notified when donors subsequently test repeatedly reactive for anti-HCV in a licensed multiantigen screening test and reactive in a licensed or investigational HCV

[1] This guidance document represents the agency's current thinking on consignee and recipient notification related to donor testing for HCV. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. The procedures cited in this guidance document are recommendations. If an establishment believes that an alternative approach would provide equivalent protection, the establishment is invited to discuss the approach with FDA for evaluation. FDA recognizes that the scientific technology for controlling the risk of transmission of HCV may continue to advance and that this document may become outdated as those advances occur. Written requests for single copies of this draft guidance document may be submitted to the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. The document may also be obtained by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800, or by fax by calling the FAX Information System at 1-888-CBER-FAX or 301-827-3844. Persons with access to the INTERNET may obtain the document using the world wide web (www). For www access, connect to CBER at "http://www.fda.gov/cber/guidelines.htm".

supplemental test. This notification would enable recipients to be informed that they had been transfused with units that may have contained HCV so that they may obtain further medical counseling**.**

II. BACKGROUND

Lookback (product retrieval and recipient notification) related to HBV, HCV and HTLV-I testing has been discussed at open public meetings, including meetings of FDA's Blood Products Advisory Committee (BPAC), on multiple occasions since October, 1989. As a response to these discussions, FDA provided detailed guidance in the July 19, 1996, memorandum on the quarantine and disposition of certain prior collections of blood and blood components from donors who subsequently test repeatedly reactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti-HBc), anti-HCV, or antibody to human T-lymphotropic virus, type I (anti-HTLV-I). The memorandum recommended that blood establishments notify consignees (such as the transfusion service, physician, fractionator, etc.) for the purpose of quarantine and eventual disposition of products made from prior collections. At that time, FDA did not recommend notification of recipients of blood from donors who subsequently test positive for anti-HCV, because no clear consensus on the public health benefit of such action had emerged.

Improvements in the treatment and management of HCV infections have occurred recently, and there is now significant evidence that an individual who is reactive for anti-HCV in a supplemental assay is likely to be infected with HCV. More specifically, in studies of blood donors tested by the supplemental RIBA 2.0 (Chiron RIBA HCV 2.0 Strip Immunoblot Assay, Chiron Corporation, Emeryville, CA), 73 to 95% of test-positive and 14 to 21% of test-indeterminate blood samples had detectable HCV RNA by PCR (1-3). [NOTE: The RIBA 2.0 assay is an immunoblot assay based on recombinant antigens of HCV.] Additionally, it is recognized that prior negative or unscreened units from donors later found to be reactive for anti-HCV may have contained HCV. At public meetings on April 24 and 25, 1997, and August 11 and 12, 1997, the PHS Advisory Committee on Blood Safety and Availability discussed recipient notification related to hepatitis C. Consistent with recommendations of the PHS Advisory Committee, on March 20, 1998, FDA issued guidance regarding such notification for implementation and comment (Federal Register 63, No. 54, 13675, Docket No. 98D-0143)**.** In response to comments received, FDA is now issuing the following revised guidance that supersedes the guidance issued on July 19, 1996**,** and replaces the guidance issued on March 20, 1998.

III. RECOMMENDATIONS

1. CURRENT TESTING

A. Quarantine of Prior Collections from Donors Who Subsequently Test Repeatedly Reactive for Anti-HCV

Whenever a donor tests repeatedly reactive in a licensed screening test for anti-HCV, blood establishments should, within 3 calendar days of obtaining the repeatedly reactive test result, identify and quarantine in-date (screened or unscreened) prior collections of Whole Blood and blood components from the same donor in inventory dating back 10 years prior to the anti-HCV repeatedly reactive donation, whenever such records exist, or to the date 12 months prior to the donor's most recent negative licensed multiantigen screening test for anti-HCV, whichever is the lesser period. Blood establishments should, within 3 calendar days, request consignees to immediately quarantine all previously distributed in-date products from such collections extending back either 10 years prior to the repeatedly reactive donation or 12 months prior to the donor's most recent negative test result using a licensed multiantigen screening test. FDA is not recommending that products which have already been pooled or further processed be quarantined. [NOTE: If additional tests on the repeatedly reactive donation are completed within 3 calendar days, and final test results provide a basis for release of units as described in section D below, then quarantine of the previously collected units is not necessary.]

B. Disposition of Units Placed in Quarantine

For donors who test repeatedly reactive for anti-HCV, additional testing on the donor's current, repeatedly reactive sample may permit release of prior collections from quarantine (see section D below). If such testing fails to be performed within 30 days or fails to meet procedures established for release of units from quarantine, then the quarantined units should be destroyed or appropriately labeled (see section D below).

C. Supplemental Testing and Notification of Consignees and Blood Recipients

Donors currently testing repeatedly reactive for anti-HCV in a licensed screening test should be further tested for anti-HCV using a licensed multiantigen supplemental test, or an investigational multiantigen supplemental test obtained for study under an appropriate IND exemption (see Figure 1). If the supplemental test result is positive, or, in the case of RIBA 2.0, if the supplemental test is either positive or indeterminate (except if an indeterminate RIBA 2.0 is followed by a negative or indeterminate RIBA 3.0 or in some cases a negative HCV EIA 3.0 as described in Recommendation 3, below), within 45 calendar days of the donor's repeatedly reactive screening test, blood establishments should notify consignees (such as hospitals, transfusion services, physicians, etc.) of previously distributed units of the donor's current test results

(including supplemental testing) and**,** if appropriate based on the subsequent test results obtained on the donor**,** the fact that the previously distributed units potentially contained HCV. This notification of consignees should be performed so that, if appropriate, recipients may be subsequently notified that they had been transfused with units that may have contained HCV (see Recommendation 5).

D. Release of Units from Quarantine

If the repeatedly reactive screening test was EIA 2.0, quarantined prior collections may be released for transfusion or further manufacture

(i) if the supplemental test using a licensed RIBA 2.0 assay was negative (quarantined prior collections should not be released if the repeatedly reactive screening test was EIA 3.0);

or

(ii) if the supplemental test using a licensed RIBA 2.0 assay was indeterminate and additional testing is performed and the results are as described in Recommendation 3.b. below.

For units previously distributed, consignees should be notified within 45 days of the results of additional testing, if performed, so that consignees may either release products (as described above), or properly dispose of products (i.e., destruction or labeling as described below).

FDA recognizes that there may be some limited uses for quarantined units from prior collections which are not suitable for release from quarantine for the product's original intended use. Such units should not be used for transfusion or for manufacturing into injectable products. FDA recommends that these units be destroyed as a general practice**;** however, in limited situations, release for research or manufacture into in-vitro diagnostic reagents may be acceptable. If released for these uses, the units should be relabeled consistent with general labeling requirements in 21 CFR 606.121 and 21 CFR 640.70. Additionally, the units should be labeled as "Biohazard" and with two cautionary statements, as follows:

"Collected from a donor who subsequently tested positive for anti-HCV. The risk of transmission of hepatitis C is present"

and either

"Caution: For Further Manufacturing Into In-Vitro Diagnostic Reagents For Which There Are No Alternative Sources"

or

"For Laboratory Research Use Only"

as appropriate.

E. Procedures and Record Keeping

Blood establishments should have written procedures to identify prior collections, to quarantine units, to notify consignees, and to perform additional testing if release of units from quarantine will be considered, whenever a repeat donor has a repeatedly reactive test for anti-HCV.

Blood establishments are reminded of their requirements under 21 CFR 606.160(d) to maintain records for five years after blood processing has been completed, or 6 months after the latest product expiration date, whichever is a later date. When there is no expiration date, records must be retained indefinitely, as required in 21 CFR 606.160(d). Records required under 21 CFR 606.160 and 21 CFR 606.165 should enable identification and quarantine of prior collections from the same donor, tracing of the distribution and disposition (including, for transfusion services, a record of transfusion) of prior collections, documentation of the quarantine of products and consignee notification, and disposition of products identified as potentially infectious based on subsequent testing. To improve the effectiveness of these activities, blood establishments should, beginning on the date this guidance is implemented, maintain adequate records of the source and disposition of all units of blood and blood products for at least 10 years from the date of disposition or 6 months after the latest product expiration date, whichever is the later date, and maintain these records in a manner which permits their rapid retrieval (e.g., within 5 working days). Blood establishments should also ensure that these records are transferred to another appropriate entity if the former establishment ceases operations for any reason.

2. PREVIOUS TESTING

A. Review of Records and Quarantine of Prior Collections

For donations tested before the date of implementation of Recommendation 1 (above) of this guidance, blood establishments should review records of donor testing dating from the facility's implementation of a licensed multiantigen screening test for anti-HCV to identify repeatedly reactive donations detected in the past ("historical repeatedly reactive donations") from donors with a record of prior donation (i.e., donations prior to the repeatedly reactive collection). Blood establishments should quarantine all such prior donations and notify consignees so that they may quarantine previously distributed units that they hold**.** [NOTE: Quarantine based on a repeatedly reactive screening test result need <u>not</u> be done if: 1) records of testing with a multiantigen supplemental test are available and review of those records can be completed within three calendar days of the date of identification of the repeatedly reactive result and the results indicate the units are acceptable for release; or 2) the unit

was collected more than 12 months prior to the donor's most recent negative licensed multiantigen screening test for anti-HCV.]

B. Notification of Consignees and Blood Recipients

If there is no record of a multiantigen supplemental test result on the historical repeatedly reactive donation (as described above), FDA recommends further action as described in Recommendation 4.

Alternatively, if there is a record of a multiantigen supplemental test result on the historical repeatedly reactive donation (see Figure 1), in which the result was positive on an investigational RIBA 3.0 assay, or was either positive or indeterminate on a licensed or investigational RIBA 2.0 assay (except if an indeterminate RIBA 2.0 result is followed by a negative or indeterminate RIBA 3.0 result or in some cases a negative HCV EIA 3.0 result, as described in Recommendation 3, below), then, as records permit, the blood establishment should identify previously distributed (screened or unscreened) units collected from the same donor dating back to January 1, 1988, or to the date 12 months prior to the donor's most recent negative licensed multiantigen screening test for anti-HCV, whichever is the lesser period. Blood establishments should notify consignees (such as hospitals, transfusion services, physicians, etc.) of such previously distributed units of the donor's test results (including supplemental testing) and, if appropriate based on the subsequent test results obtained on the donor, the fact that the previously distributed units potentially contained HCV. This notification of consignees should be performed so that, if appropriate, recipients may be subsequently notified that they had been transfused with units that may have contained HCV (see Recommendation 5). This notification of consignees need not be done if the consignee can document that records of product distribution for transfusion are no longer available for the time period during which the unit was released for transfusion.

Blood establishments should begin notification of consignees as soon as feasible and no later than 6 months from the date of issuance of this guidance. FDA recommends that this notification be completed within 18 months of the date of publication of this guidance.

C. Release of Units from Quarantine

If the repeatedly reactive screening test was EIA 2.0, quarantined prior collections may be released for transfusion or further manufacture

(i) if the supplemental test using a licensed RIBA 2.0 assay was negative (quarantined prior collections should not be released if the repeatedly reactive screening test was EIA 3.0);

or

(ii) if the supplemental test using a licensed RIBA 2.0 assay was indeterminate and additional testing is performed and the results are as described in Recommendation 3.b. below.

For units previously distributed, consignees should be notified within 30 days of the results of additional testing, if performed, so that consignees may either release products (as described above), or properly dispose of products (i.e., destruction or labeling as described below).

FDA recognizes that there may be some limited uses for quarantined units from prior collections which are not suitable for release from quarantine for the product's original intended use. Such units should not be used for transfusion or for manufacturing into injectable products. FDA recommends that these units be destroyed as a general practice; however, in limited situations, release for research or manufacture into in-vitro diagnostic reagents may be acceptable. If released for these uses, the units should be relabeled consistent with general labeling requirements in 21 CFR 606.121 and 21 CFR 640.70. Additionally, the units should be labeled as "Biohazard" and with two cautionary statements, as follows:

"Collected from a donor who subsequently tested positive for anti-HCV. The risk of transmission of hepatitis C is present"

and either

"Caution: For Further Manufacturing Into In-Vitro Diagnostic Reagents For Which There Are No Alternative Sources"

or

"For Laboratory Research Use Only"

as appropriate.

3. ADDITIONAL TESTING FOLLOWING AN INDETERMINATE RIBA 2.0 TEST RESULT

In the case of a current repeatedly reactive donation (see Recommendation 1) or a historical repeatedly reactive donation (as described in Recommendation 2), if the supplemental test result of record is an <u>indeterminate</u> test result obtained using Chiron's RIBA 2.0 assay, the original stored sample or a fresh sample from the donor may be tested again according to the following options (see Figure 1):

a. Using Chiron's investigational RIBA 3.0 assay (under an appropriate IND exemption).

(i) If the additional test by RIBA 3.0 is positive, then consignee notification for the purpose of recipient notification as described in Recommendations 1 and 2 should be performed, and the previously distributed units should be destroyed or labeled consistent with Recommendation 1.D. or 2.C. above.

(ii) If the test result is negative or indeterminate, consignees should be notified, not for the purpose of recipient notification, but so that they may destroy or label previously distributed units consistent with Recommendation 1.D. or 2.C. above. [NOTE: This alternative is based on current research that indicates absence of PCR reactivity for HCV RNA in RIBA 2.0 indeterminate/RIBA 3.0 negative samples (4), and infrequent (0.5% to 4%) PCR reactivity in RIBA 2.0 indeterminate/RIBA 3.0 indeterminate samples (4,5).] In this situation, quarantined prior collections should not be released even if the RIBA 3.0 assay is negative. (FDA does not recommend release of quarantined units despite a negative result on RIBA 3.0 due to the current investigational status of the RIBA 3.0 assay.)

b. Using a licensed HCV EIA 3.0 test. [NOTE: This option is only available if the original repeatedly reactive screening test result was obtained using an HCV EIA 2.0 test.]

(i) If the additional test result by EIA 3.0 is negative, consignees should be notified, not for the purpose of recipient notification, but so that quarantined prior collections may be released. [NOTE: This alternative is based on current research that indicates the very low probability of RIBA 3.0 positivity (0.8%) or HCV RNA positivity (none detected) in RIBA 2.0 indeterminate/EIA 3.0 negative samples (6-8).]

(ii) If the additional test by EIA 3.0 is repeatedly reactive, then consignee notification for the purpose of recipient notification as described in Recommendations 1 and 2 should be performed and the previously distributed units should be destroyed or labeled consistent with Recommendation 1.D. or 2.C. above. Alternatively, the sample may be tested again using RIBA 3.0. If the result is positive, then consignee notification for the purpose of recipient notification as described in Recommendations 1 and 2 should be performed, and the previously distributed units should be destroyed or labeled consistent with Recommendation 1.D. or 2.C. above. If the test result is negative or indeterminate, consignees should be notified, not for the purpose of recipient notification, but so that they may destroy or label previously distributed units consistent with Recommendation 1.D. or 2.C. above. In this situation, quarantined prior collections should not be released even if the RIBA 3.0 assay is negative. (FDA does not recommend release of quarantined units despite a negative result on RIBA 3.0 due to the current investigational status of the RIBA 3.0 assay.)

4. ADDITIONAL TESTING IN THE CASE OF A HISTORICAL REPEATEDLY REACTIVE RESULT WITH NO RECORD OF A SUPPLEMENTAL TEST

In the case of donations that tested repeatedly reactive in a multiantigen anti-HCV screening assay performed prior to the date of implementation of this guidance, as described in Recommendation 2, where there is no record of a supplemental assay result, and where units were distributed for transfusion from any prior donation dating back to January 1, 1988, blood establishments should perform additional testing on a stored sample (i.e., a previously frozen serum or plasma sample from the repeatedly reactive donation) or on a newly acquired donor sample (see Figure 2). Such additional testing (as described below) should be performed within 6 months of the date of publication of this guidance. Results of such additional testing should be treated consistent with Recommendations 2 and 3 above, regarding test results, to determine the need for recipient notification and disposition of quarantined products.

a. If the repeatedly reactive result was obtained using an HCV EIA 2.0 test, the blood establishment should retrieve a stored sample or obtain a fresh blood sample from the donor and perform either
   (i) a currently licensed, or, if available under an IND exemption, an investigational multiantigen supplemental test for antibodies to HCV. Notification of consignees for the purpose of recipient notification, if appropriate (i.e., consistent with recommendations based on test results as described in section 2.B.), and disposition of previously distributed units (see below) should be conducted within 30 days of obtaining the additional test result; or
   (ii) a currently licensed HCV EIA 3.0 screening test. If the result is negative, consignee notification for the purpose of recipient notification need not be performed, but consignees should be notified of the additional test result to permit release of quarantined prior collections. If the result is repeatedly reactive, then consignee notification for the purpose of recipient notification, if appropriate (i.e., consistent with recommendations based on test results as described in section 3.b.(ii)), and disposition of previously distributed units as described in Recommendation 2 should be conducted, unless a licensed or investigational (if available under IND exemption) multiantigen supplemental test for antibodies to HCV can be performed. This notification should be carried out within 30 days of obtaining the additional test result. If a licensed or investigational multiantigen supplemental test for antibodies to HCV is performed, notification of consignees for the purpose of recipient notification, if appropriate (i.e., consistent with recommendations based on test results as described in section 2.B.), and disposition of previously distributed units (see below) should be conducted within 30 days of obtaining the additional test result.

b. If the repeatedly reactive result was obtained using an HCV EIA 3.0 test, the blood establishment should retrieve a stored sample from the repeatedly reactive donation or obtain a fresh blood sample from the donor and perform a currently licensed, or, if available under an IND exemption, an investigational multiantigen supplemental test for antibodies to HCV. Notification of consignees for the purpose of recipient notification, if appropriate (i.e., consistent with recommendations based on test results as described in section 2.B.), and disposition of previously distributed units (see below) should be conducted within 30 days of obtaining the additional test result.

c. If the blood establishment does not retest a previously stored sample from the repeatedly reactive donation and does not test a fresh sample from the donor, then consignees of units collected from the same donor dating back to January 1, 1988, or the date 12 months prior to the donor's most recent negative licensed multiantigen screening test for anti-HCV, whichever is the lesser period, should be notified of prior receipt of a unit that potentially contained HCV and of the donor's test results, including lack of availability of results from supplemental testing, so that recipient notification may be performed and previously distributed units may be destroyed or labeled consistent with Recommendation 2 above. This notification should be completed within 18 months of the date of publication of this guidance.

Quarantined prior collections may be released if the result of the licensed HCV EIA 3.0 (see a(ii) above) is negative. Quarantined prior collections may be released when an EIA 2.0 repeatedly reactive result is followed by a negative licensed supplemental test (RIBA 2.0) (see a(i) above); however, they should <u>not</u> be released when an EIA 3.0 repeatedly reactive result is followed by a negative RIBA 2.0 (see b above). Disposition of such units should be consistent with Recommendation 2 above.

5. NOTIFICATION OF BLOOD RECIPIENTS

Any hospital or transfusion service or other appropriate entity acting on behalf of a blood establishment that is notified of the prior receipt of a unit that potentially contained HCV should take the following actions:

a. Promptly attempt to notify the patient. Notification may be carried out in either of two ways:

(i) Notify the patient directly, in which case the physician of record or the physician who ordered the blood or blood product that potentially contained HCV should be informed concurrently of the notification; or

(ii) Notify the physician of record (i.e., the attending physician or the physician who ordered the blood or blood product) that a transfused unit potentially contained HCV and ask the physician to immediately notify the patient, or other individual as described under paragraph f of this section, of the need for HCV testing and counseling. If the

physician is unavailable, declines to make the notification, or later informs the hospital that he or she was unable to notify the patient, the hospital or transfusion service should promptly attempt to notify the patient or other individual as described under paragraph f, whenever such additional efforts are feasible (e.g., if the physician made only a single attempt at notification, the hospital or transfusion service should pursue additional attempts, as previously described).

b. In the patient's medical record or in the hospital's or transfusion service's permanent records, document the notification, the attempts at notification, and the reasons for all failures to notify (for example, if the patient refuses to accept the notification information or is deceased).

c. The notification effort based on donor testing completed after the date of implementation of Recommendation 1 of this guidance (above) should begin when the blood establishment notifies the hospital or transfusion service of the prior receipt of a unit that potentially contained HCV and should include a minimum of three attempts and be completed within a maximum of 12 weeks, unless

(i) the patient (or other individual as permitted under paragraph f) is located and notified; or
(ii) the hospital or transfusion service is unable to locate or notify the patient and documents the extenuating circumstances beyond the hospital's or transfusion service's control that caused the notification effort to be discontinued prior to 12 weeks or to be delayed.

d. The notification effort based on donor testing that occurred before the date of implementation of Recommendation 1 of this guidance (above) should begin when the blood establishment notifies the hospital or transfusion service of the prior receipt of a unit that potentially contained HCV, should include a minimum of three attempts to make the notification, and should be completed within one year of the date on which the hospital or transfusion service received notification from the blood establishment.

e. Recipient notification should include the following information:

(i) A basic explanation of the need for HCV testing and counseling;
(ii) Sufficient oral or written information so that the transfusion recipient can make an informed decision about whether to obtain HCV testing and counseling; and
(iii) A list of programs or places where the patient can obtain HCV testing and counseling, including any requirements or restrictions the program may impose.

f. If the patient has been judged incompetent by a state court, the hospital, transfusion service or physician should notify a legal representative designated in accordance with state law. If the patient is competent, but state law permits a legal representative or relative to receive the information on the patient's behalf, the

hospital, transfusion service or physician should notify the patient or his or her legal representative or relative. If the patient is a minor (at the time of the notification), the hospital, transfusion service or physician should notify the patient's legal representative or relative. If the patient is deceased, the hospital, transfusion service or physician may discontinue the notification process.

To achieve this result, hospitals or other entities should, beginning on the date this guidance is implemented, maintain adequate records of the source and disposition of all units of blood and blood products for at least 10 years from the date of disposition or 6 months after the latest product expiration date, whichever is the later date, and maintain these records in a manner that permits their rapid retrieval, as required in 21 CFR 606.165(a) (e.g., within 5 working days). Hospitals or other entities also should ensure that these records are transferred to another appropriate entity if the former establishment ceases operations for any reason.

IV. IMPLEMENTATION

The recommendations contained in this guidance document may be implemented immediately without prior approval by FDA. Licensed establishments implementing these recommendations should submit in their annual reports a statement indicating the date that revised SOP's consistent with the recommendations have been established and implemented.

V. REFERENCES

1. Sayers, M.H., and Gretch, D.R. Recombinant immunoblot and polymerase chain reaction testing in volunteer whole blood donors screened by a multiantigen assay for hepatitis C virus antibodies. *Transfusion* 33:809-813 (1993).

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4. Alter, H. et al. (Unpublished data). Department of Transfusion Medicine, National Institutes of Health, Bethesda, Maryland.

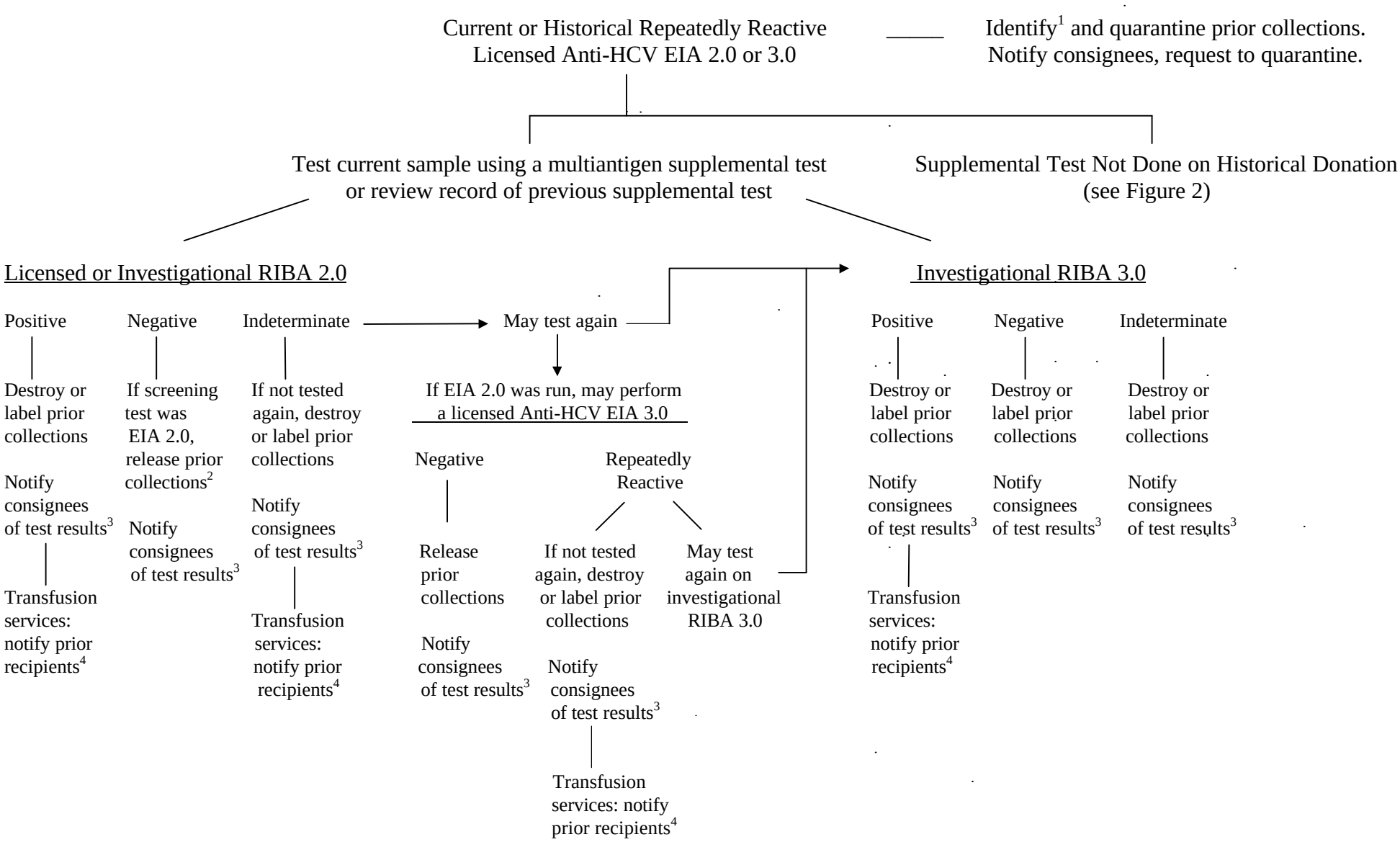
5. Dow, B.C. et al. Relevance of RIBA-3 supplementary test to HCV PCR positivity and genotypes for HCV confirmation of blood donors. *Journal of Medical Virology* 49:132-136 (1996).

6. Uyttendaele, S. et al. Evaluation of third-generation screening and confirmatory assays for HCV antibodies. *Vox Sanguinis* 66:122-129 (1994).

7. Destree, M.J. et al. Evaluation of the Ortho HCV 3.0 assay on a repository of HCV 2.0 positive samples. *Transfusion* 37(Suppl):3S (1997).

8. Tobler, L.H. et al. Use of HCV Version 3 (EIA3) to determine lookback status of EIA2 reactive(R)/ RIBA HCV 2.0 SIA (RIBA 2) indeterminate (IND) donors. 1998 AABB Annual Meeting abstract (to be presented).

Figure 1 **FDA Recommendations for Quarantine and Disposition of Units from Prior Collections, Supplemental Testing, and Notification of Consignees and Blood Recipients of Donor Test Results for Antibody to Hepatitis C Virus (Anti-HCV)**



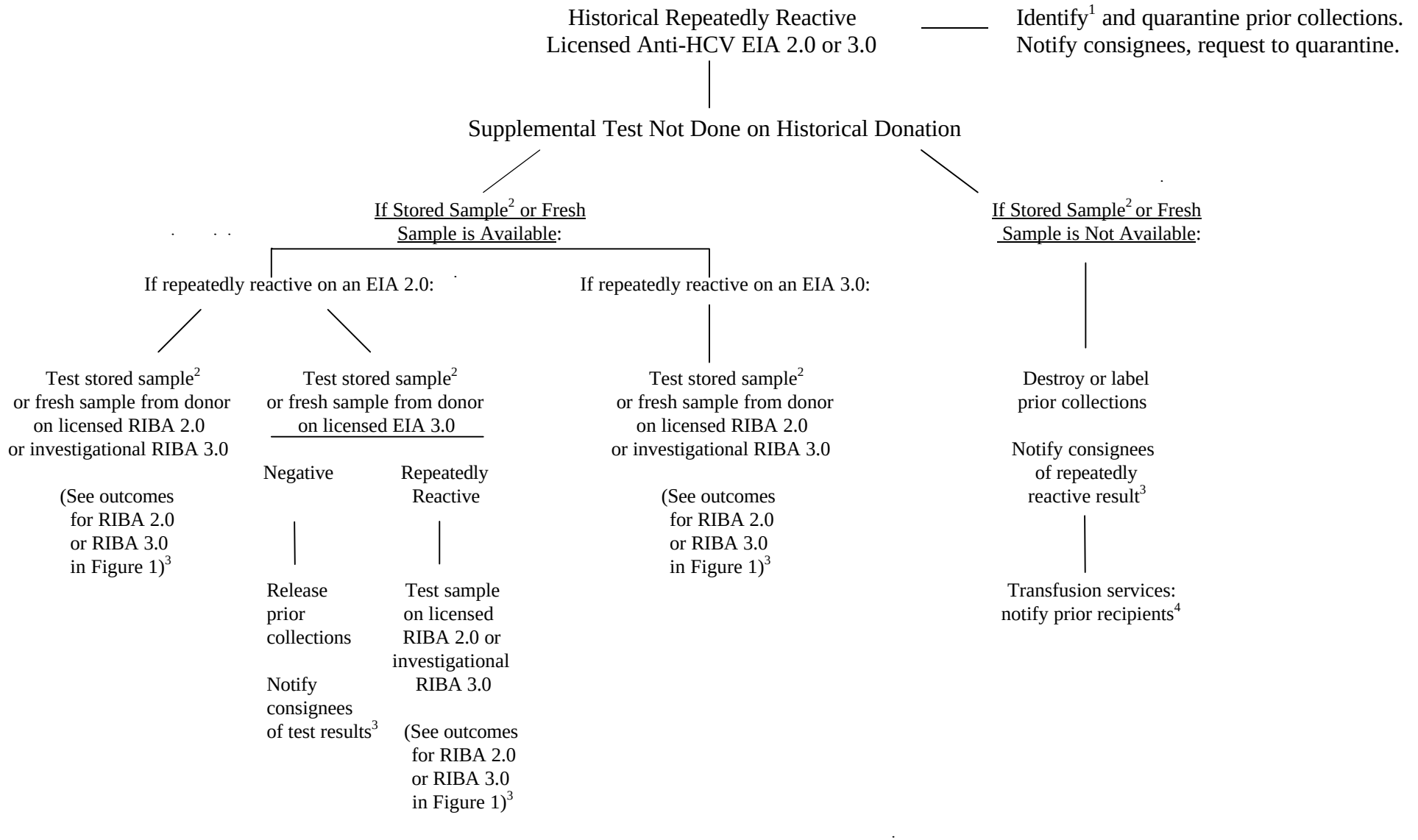
[1] Previously distributed units from the same donor dating back 10 years (for a current repeatedly reactive result) or to 1/1/88 (for a historical repeatedly reactive result), or to the date 12 months prior to the most recent negative licensed multiantigen screening test should be identified.

[2] If the repeatedly reactive screening test was EIA 3.0 and the negative supplemental test was RIBA 2.0, destroy or label prior collections.

[3] Notify consignees within 45 days of the current repeatedly reactive result, or as soon as feasible for a historical repeatedly reactive result. If a supplemental test was not done (see Fig. 2) and additional testing is now performed on a stored or fresh sample, notify consignees within 30 days of obtaining the additional test result (see Fig. 2, footnote 3).

[4] Transfusion services should identify and notify recipients of prior collections dating back to 1/1/88 (some exceptions apply).

Figure 2 **FDA Recommendations for Quarantine and Disposition of Units from Prior Collections, Supplemental Testing, and Notification of Consignees and Blood Recipients of Donor Test Results for Antibody to Hepatitis C Virus (Anti-HCV) (Cont.)**



[1] Previously distributed units from the same donor dating back to 1/1/88, or to the date 12 months prior to the most recent negative multiantigen screening test should be identified.

[2] A previously frozen serum or plasma sample from the repeatedly reactive donation.

[3] Notify consignees within 30 days of obtaining the additional test result, or within 18 months of the issuance of this guidance for a historical repeatedly reactive result if no stored sample or fresh donor sample is available.

[4] Transfusion services should identify and notify recipients of prior collections dating back to 1/1/88 (some exceptions apply).